

10/758,589

9/14/2007

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Welcome to STN International! Enter x:x

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PASSWORD:

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* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page for STN Seminar Schedule - N. America
NEWS 2 MAY 01 New CAS web site launched
NEWS 3 MAY 08 CA/CAPLUS Indian patent publication number format defined
NEWS 4 MAY 14 RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS 5 MAY 21 BIOSIS reloaded and enhanced with archival data
NEWS 6 MAY 21 TOXCENTER enhanced with BIOSIS reload
NEWS 7 MAY 21 CA/CAPLUS enhanced with additional kind codes for German patents
NEWS 8 MAY 22 CA/CAPLUS enhanced with IPC reclassification in Japanese patents
NEWS 9 JUN 27 CA/CAPLUS enhanced with pre-1967 CAS Registry Numbers
NEWS 10 JUN 29 STN Viewer now available
NEWS 11 JUN 29 STN Express, Version 8.2, now available
NEWS 12 JUL 02 LEMBASE coverage updated
NEWS 13 JUL 02 LMEDLINE coverage updated
NEWS 14 JUL 02 SCISEARCH enhanced with complete author names
NEWS 15 JUL 02 CHEMCATS accession numbers revised
NEWS 16 JUL 02 CA/CAPLUS enhanced with utility model patents from China
NEWS 17 JUL 16 CAPLUS enhanced with French and German abstracts
NEWS 18 JUL 18 CA/CAPLUS patent coverage enhanced
NEWS 19 JUL 26 USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 20 JUL 30 USGENE now available on STN
NEWS 21 AUG 06 CAS REGISTRY enhanced with new experimental property tags
NEWS 22 AUG 06 BEILSTEIN updated with new compounds
NEWS 23 AUG 06 FSTA enhanced with new thesaurus edition
NEWS 24 AUG 13 CA/CAPLUS enhanced with additional kind codes for granted patents
NEWS 25 AUG 20 CA/CAPLUS enhanced with CAS indexing in pre-1907 records
NEWS 26 AUG 27 Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 27 AUG 27 USPATOLD now available on STN
NEWS 28 AUG 28 CAS REGISTRY enhanced with additional experimental spectral property data

NEWS 29 SEP 07 STN AnaVist, Version 2.0, now available with Derwent World Patents Index

NEWS EXPRESS 05 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 05 SEPTEMBER 2007.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 15:40:28 ON 12 SEP 2007

=> file registry

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 15:40:40 ON 12 SEP 2007

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 11 SEP 2007 HIGHEST RN 946658-01-1

DICTIONARY FILE UPDATES: 11 SEP 2007 HIGHEST RN 946658-01-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

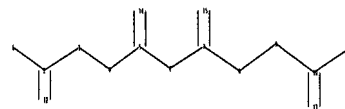
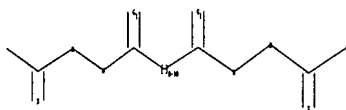
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

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Uploading C:\Program Files\Stnexp\Queries\10758589_clm1.str



chain nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

chain bonds :

1-2 2-3 2-12 3-4 4-5 5-6 5-14 6-7 7-8 7-15 8-9 9-10 10-11 10-13

exact/norm bonds :

2-3 2-12 3-4 4-5 5-14 7-8 7-15 8-9 9-10 10-13

exact bonds :

1-2 5-6 6-7 10-11

G1:O,S

Match level :

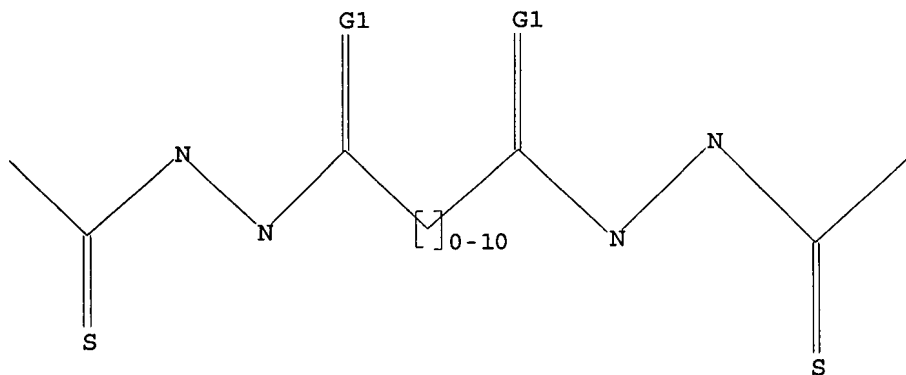
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



G1 O,S

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full

FULL SEARCH INITIATED 15:40:56 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 186 TO ITERATE

100.0% PROCESSED 186 ITERATIONS

17 ANSWERS

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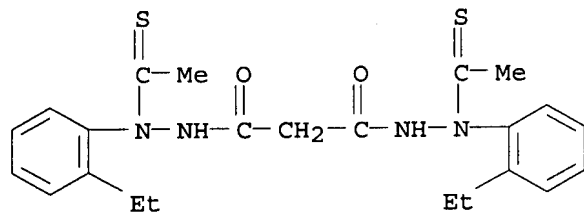
L2 17 SEA SSS FUL L1

=> d scan

L2 17 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN Propanedioic acid, bis[2-(2-ethylphenyl)-2-(1-thioxoethyl)hydrazide] (9CI)

MF C23 H28 N4 O2 S2



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

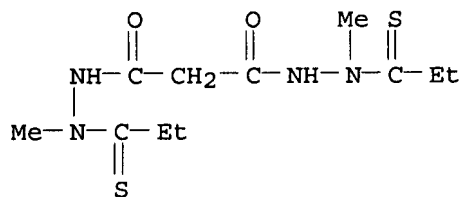
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L2 17 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN Propanedioic acid, 1,3-bis[2-methyl-2-(1-thioxopropyl)hydrazide]

MF C11 H20 N4 O2 S2

CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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=> file medline caplus wpids uspatfull
COST IN U.S. DOLLARS

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| 172.55 | 172.76 |

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 15:41:45 ON 12 SEP 2007

FILE 'CAPLUS' ENTERED AT 15:41:45 ON 12 SEP 2007

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FILE 'WPIDS' ENTERED AT 15:41:45 ON 12 SEP 2007

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FILE 'USPATFULL' ENTERED AT 15:41:45 ON 12 SEP 2007

CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

=> s 12

SAMPLE SEARCH INITIATED 15:41:50 FILE 'WPIDS'

SAMPLE SCREEN SEARCH COMPLETED - 16 TO ITERATE

100.0% PROCESSED 16 ITERATIONS

2 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 41 TO 279

PROJECTED ANSWERS: 2 TO 62

L3 24 L2

=> s 13 and (?cancer? or ?tumor?)

L4 21 L3 AND (?CANCER? OR ?TUMOR?)

=> s 14 and py<2004

2 FILES SEARCHED...

L5 5 L4 AND PY<2004

=> d 15 1-5 ibib, abs, hitstr

L5 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:58056 CAPLUS

DOCUMENT NUMBER: 138:122397

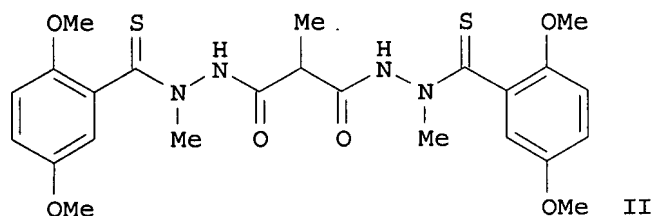
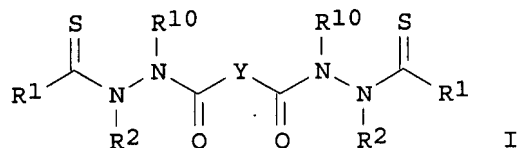
TITLE: Process for the preparation of bis(thiohydrazide)
derivatives used as Taxol enhancers

INVENTOR(S): Chen, Shoujun; Sun, Lijun; Xia, Zhi-Qiang; Koya,
Keizo; Ono, Mitsunori

PATENT ASSIGNEE(S): SBR Pharmaceuticals Corp., USA

SOURCE: PCT Int. Appl., 57 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

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| WO 2003006429 | A1 | 20030123 | WO 2002-US21716 | 20020710 <-- |
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| TW 252847 | B | 20060411 | TW 2002-91115205 | 20020709 |
| CA 2453415 | A1 | 20030123 | CA 2002-2453415 | 20020710 <-- |
| AU 2002316625 | A1 | 20030129 | AU 2002-316625 | 20020710 <-- |
| US 2003069225 | A1 | 20030410 | US 2002-193076 | 20020710 <-- |
| US 6825235 | B2 | 20041130 | | |
| EP 1406868 | A1 | 20040414 | EP 2002-746946 | 20020710 |
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| JP 2004534847 | T | 20041118 | JP 2003-512201 | 20020710 |
| CN 1553893 | A | 20041208 | CN 2002-817724 | 20020710 |
| NO 2004000053 | A | 20040210 | NO 2004-53 | 20040107 |
| MX 2004PA00245 | A | 20050307 | MX 2004-PA245 | 20040109 |
| IN 2004DN00077 | A | 20060224 | IN 2004-DN77 | 20040112 |
| US 2004229952 | A1 | 20041118 | US 2004-807919 | 20040324 |
| US 7074952 | B2 | 20060711 | | |
| US 2006281811 | A1 | 20061214 | US 2006-440429 | 20060524 |
| AU 2006203689 | A1 | 20060914 | AU 2006-203689 | 20060824 |
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| | | | US 2001-304318P | P 20010710 |
| | | | US 2002-193076 | A1 20020710 |
| | | | WO 2002-US21716 | W 20020710 |
| | | | US 2004-807919 | A1 20040324 |
| OTHER SOURCE(S): CASREACT 138:122397; MARPAT 138:122397 | | | | |
| GI | | | | |



AB Disclosed is a method of preparing bis(thiohydrazide) I [R1-2 = aliphatic, aryl,

etc.; R10 = H, alkyl; Y = bond, hydrocarbyl]. The method comprises reacting a hydrazide with a thionation reagent followed by reaction of the thiohydrazide with Z-C(O)-Y-C(O)-Z or HO-C(O)-Y-C(O)-OH [Z = leaving group; Y is as defined above] and a carboxylic acid activating agent to produce I. For instance, 2,5-dimethoxybenzoic acid is coupled to methylhydrazine (CH₂Cl₂, DCC, DMAP); the resulting hydrazide is treated with Lawesson's reagent and the product reacted with 2-methylmalonic acid (DMF, DCC) to give II. I enhance the anti-cancer activity of taxol and analogs thereof.

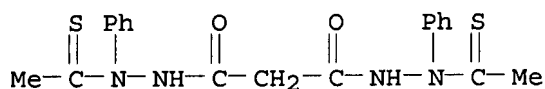
IT 488831-49-8P 488831-53-4P 488831-54-5P
488831-55-6P 488831-56-7P 488831-57-8P
488831-58-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(process for preparation of bis(thiohydrazide) derivs. used as Taxol enhancers)

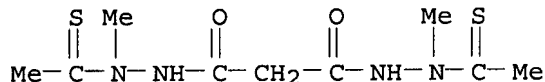
RN 488831-49-8 CAPLUS

CN Propanedioic acid, 1,3-bis[2-phenyl-2-(1-thioxoethyl)hydrazide] (CA INDEX NAME)



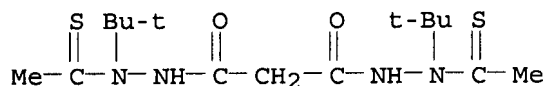
RN 488831-53-4 CAPLUS

CN Propanedioic acid, 1,3-bis[2-methyl-2-(1-thioxoethyl)hydrazide] (CA INDEX NAME)



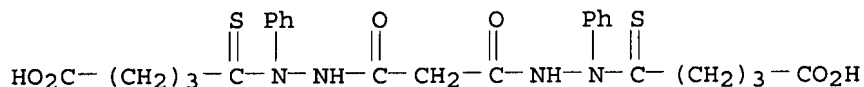
RN 488831-54-5 CAPLUS

CN Propanedioic acid, 1,3-bis[2-(1,1-dimethylethyl)-2-(1-thioxoethyl)hydrazide] (CA INDEX NAME)



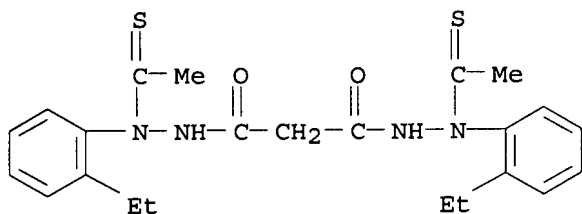
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CN Propanedioic acid, bis[2-(4-carboxy-1-thioxobutyl)-2-phenylhydrazide] (9CI) (CA INDEX NAME)



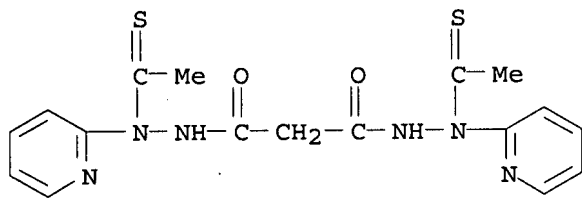
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CN Propanedioic acid, bis[2-(2-ethylphenyl)-2-(1-thioxoethyl)hydrazide] (9CI) (CA INDEX NAME)



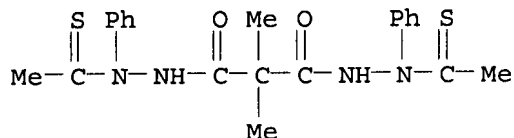
RN 488831-57-8 CAPLUS

CN Propanedioic acid, bis[2-(2-pyridinyl)-2-(1-thioxoethyl)hydrazide] (9CI)
(CA INDEX NAME)



RN 488831-58-9 CAPLUS

CN Propanedioic acid, dimethyl-, bis[2-phenyl-2-(1-thioxoethyl)hydrazide]
(9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:58055 CAPLUS

DOCUMENT NUMBER: 138:122396

TITLE: Preparation of bis(thiohydrazide) derivatives as Taxol enhancer compounds

INVENTOR(S): Koya, Keizo; Sun, Lijun; Chen, Shoujun; Tatsuta, Noriaki; Wu, Yaming; Ono, Mitsunori; Xia, Zhi-Qiang

PATENT ASSIGNEE(S): SBR Pharmaceuticals Corp., USA

SOURCE: PCT Int. Appl., 93 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

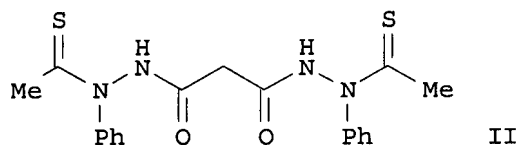
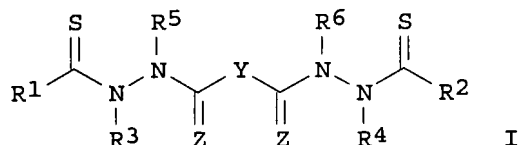
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PATENT INFORMATION:

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| ZA 2004001054 | A | 20050622 | ZA 2004-1054 | 20040209 |
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| | | | US 2002-193075 | A1 20020710 |
| | | | US 2002-193639 | A1 20020710 |
| | | | WO 2002-US21714 | W 20020710 |
| | | | US 2004-803798 | A1 20040318 |
| | | | US 2004-846152 | A1 20040514 |
| OTHER SOURCE(S): MARPAT 138:122396 | | | | |
| GI | | | | |



AB Title compds. I [Y = bond, phenylene, hydrocarbyl or taken together with both >C=Z groups is aromatic; R1-2 = (un)substituted aryl; R3-4 = H, alkyl, aryl; R5-6 = H, alkyl, aryl; Z = O, with provisions] and analogs are prepared For instance, phenylhydrazine was reacted with Et malonate (xylene, reflux) and the resulting bis(hydrazide), acetylated (Ac2O, HClO4) and treated with HCl/acetone/Na2S to afford II. The combination of example compds. and paclitaxel administered to mice with tumors (MDA-435) results in greater tumor reduction than either active component given alone.

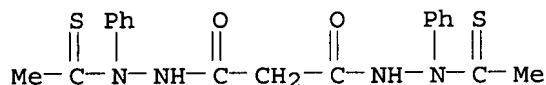
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of bis(thiohydrazide) derivs. as Taxol enhancer compds. for the
treatment of cancer)

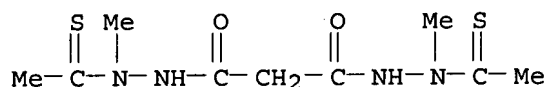
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CN Propanedioic acid, 1,3-bis[2-phenyl-2-(1-thioxoethyl)hydrazide] (CA INDEX
NAME)



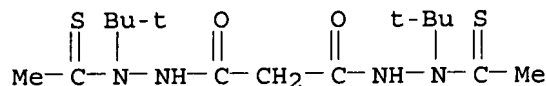
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NAME)



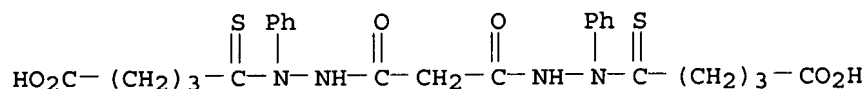
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thioxoethyl)hydrazide] (CA INDEX NAME)



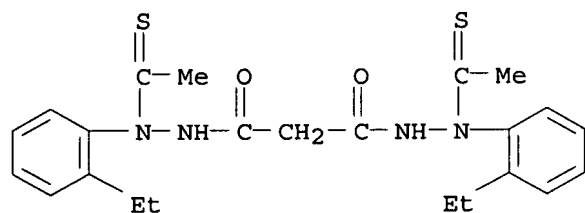
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CN Propanedioic acid, bis[2-(4-carboxy-1-thioxobutyl)-2-phenylhydrazide]
(9CI) (CA INDEX NAME)



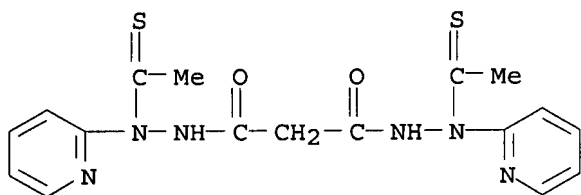
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CN Propanedioic acid, bis[2-(2-ethylphenyl)-2-(1-thioxoethyl)hydrazide] (9CI)
(CA INDEX NAME)



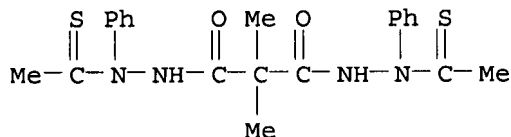
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(CA INDEX NAME)



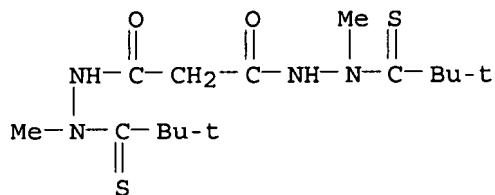
RN 488831-58-9 CAPLUS

CN Propanedioic acid, dimethyl-, bis[2-phenyl-2-(1-thioxoethyl)hydrazide]
(9CI) (CA INDEX NAME)



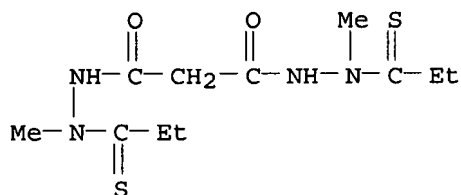
RN 488831-60-3 CAPLUS

CN Propanedioic acid, 1,3-bis[2-(2,2-dimethyl-1-thioxopropyl)-2-methylhydrazide] (CA INDEX NAME)



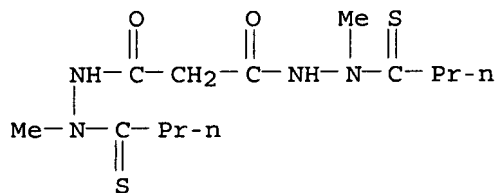
RN 488831-61-4 CAPLUS

CN Propanedioic acid, 1,3-bis[2-methyl-2-(1-thioxopropyl)hydrazide] (CA INDEX NAME)



RN 488831-65-8 CAPLUS

CN Propanedioic acid, 1,3-bis[2-methyl-2-(1-thioxobutyl)hydrazide] (CA INDEX NAME)



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 5 USPATFULL on STN

ACCESSION NUMBER: 2003:174066 USPATFULL
TITLE: Taxol enhancer compounds
INVENTOR(S): Koya, Keizo, Brookline, MA, UNITED STATES
Sun, Lijun, Harvard, MA, UNITED STATES
Chen, Shoujun, Billerica, MA, UNITED STATES
Tatsuta, Noriaki, Lexington, MA, UNITED STATES
Wu, Yaming, Lexington, MA, UNITED STATES
Ono, Mitsunori, Lexington, MA, UNITED STATES
PATENT ASSIGNEE(S): Shionogi BioResearch Corp., Lexington, MA (U.S. corporation)

| | NUMBER | KIND | DATE | |
|---------------------|----------------|------|----------|------|
| PATENT INFORMATION: | US 2003119914 | A1 | 20030626 | <-- |
| | US 6800660 | B2 | 20041005 | |
| APPLICATION INFO.: | US 2002-193075 | A1 | 20020710 | (10) |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2001-304252P | 20010710 (60) |
| | US 2002-361946P | 20020306 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133 | |
| NUMBER OF CLAIMS: | 117 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 26 Drawing Page(s) | |
| LINE COUNT: | 2227 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed is a compound represented by the Structural Formula (I):
##STR1##

Y is a covalent bond, a phenylene group or a substituted or unsubstituted straight chained hydrocarbonyl group. In addition, Y, taken together with both >C.dbd.Z groups to which it is bonded, is a substituted or unsubstituted aromatic group. Preferably, Y is a covalent bond or --C(R.sub.7R.sub.8)--.

R.sub.1 and R.sub.2 are independently an aryl group or a substituted aryl group, R.sub.3 and R.sub.4 are independently --H, an aliphatic group, a substituted aliphatic group, an aryl group or a substituted aryl group.

R.sub.5-R.sub.6 are independently --H, an aliphatic group, a substituted aliphatic group, an aryl group or a substituted aryl group.

R.sub.7 and R.sub.8 are each independently --H, an aliphatic or substituted aliphatic group, or R.sub.7 is --H and R.sub.8 is a substituted or unsubstituted aryl group, or, R.sub.7 and R.sub.8, taken together, are a C2-C6 substituted or unsubstituted alkylene group.

Z is .dbd.O or .dbd.S.

Also disclosed are pharmaceutical compositions comprising the compound of the present invention and a pharmaceutically acceptable carrier or diluent. Also disclosed is a method of treating a subject with cancer by administering to the subject a compound of Structural Formula (I) in combination with taxol or an analog of taxol.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 488831-49-8P 488831-53-4P 488831-54-5P
488831-55-6P 488831-56-7P 488831-57-8P

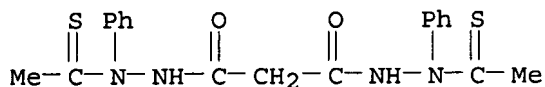
488831-58-9P 488831-60-3P 488831-61-4P

488831-65-8P

(preparation of bis(thiohydrazide) derivs. as Taxol enhancer compds. for the treatment of cancer)

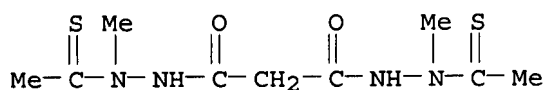
RN 488831-49-8 USPATFULL

CN Propanedioic acid, 1,3-bis[2-phenyl-2-(1-thioxoethyl)hydrazide] (CA INDEX NAME)



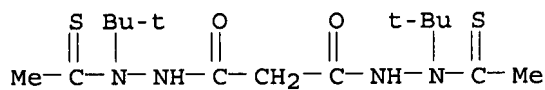
RN 488831-53-4 USPATFULL

CN Propanedioic acid, 1,3-bis[2-methyl-2-(1-thioxoethyl)hydrazide] (CA INDEX NAME)



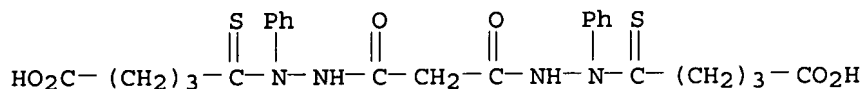
RN 488831-54-5 USPATFULL

CN Propanedioic acid, 1,3-bis[2-(1,1-dimethylethyl)-2-(1-thioxoethyl)hydrazide] (CA INDEX NAME)



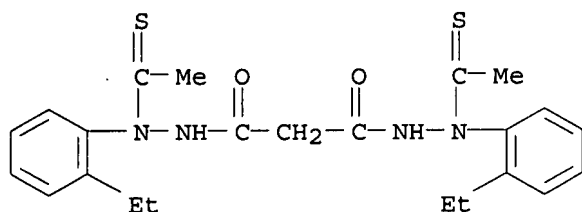
RN 488831-55-6 USPATFULL

CN Propanedioic acid, bis[2-(4-carboxy-1-thioxobutyl)-2-phenylhydrazide] (9CI) (CA INDEX NAME)



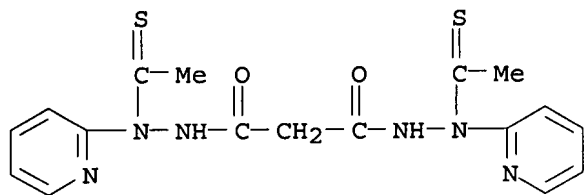
RN 488831-56-7 USPATFULL

CN Propanedioic acid, bis[2-(2-ethylphenyl)-2-(1-thioxoethyl)hydrazide] (9CI) (CA INDEX NAME)



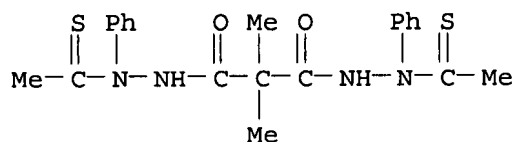
RN 488831-57-8 USPATFULL

CN Propanedioic acid, bis[2-(2-pyridinyl)-2-(1-thioxoethyl)hydrazide] (9CI) (CA INDEX NAME)



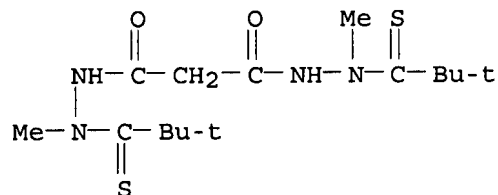
RN 488831-58-9 USPATFULL

CN Propanedioic acid, dimethyl-, bis[2-phenyl-2-(1-thioxoethyl)hydrazide]
(9CI) (CA INDEX NAME)



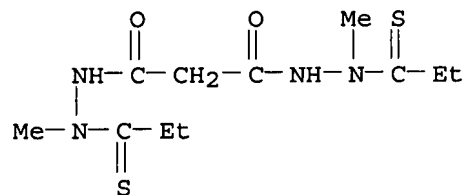
RN 488831-60-3 USPATFULL

CN Propanedioic acid, 1,3-bis[2-(2,2-dimethyl-1-thioxopropyl)-2-methylhydrazide] (CA INDEX NAME)



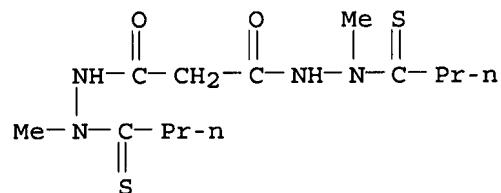
RN 488831-61-4 USPATFULL

CN Propanedioic acid, 1,3-bis[2-methyl-2-(1-thioxopropyl)hydrazide] (CA INDEX NAME)



RN 488831-65-8 USPATFULL

CN Propanedioic acid, 1,3-bis[2-methyl-2-(1-thioxobutyl)hydrazide] (CA INDEX NAME)



L5 ANSWER 4 OF 5 USPATFULL on STN

ACCESSION NUMBER: 2003:100114 USPATFULL
TITLE: Synthesis of taxol enhancers
INVENTOR(S): Chen, Shoujun, Billerica, MA, UNITED STATES
Sun, Lijun, Harvard, MA, UNITED STATES
Xia, Zhi-Qiang, Dedham, MA, UNITED STATES
Koya, Keizo, Brookline, MA, UNITED STATES
Ono, Mitsunori, Lexington, MA, UNITED STATES
PATENT ASSIGNEE(S): Shionogi BioResearch Corp., Lexington, MA (U.S.
corporation)

| | NUMBER | KIND | DATE | |
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| PATENT INFORMATION: | US 2003069225 | A1 | 20030410 | <-- |
| | US 6825235 | B2 | 20041130 | |
| APPLICATION INFO.: | US 2002-193076 | A1 | 20020710 | (10) |

| | NUMBER | DATE |
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| PRIORITY INFORMATION: | US 2001-304318P | 20010710 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133 | |
| NUMBER OF CLAIMS: | 60 | |
| EXEMPLARY CLAIM: | 1 | |
| LINE COUNT: | 1181 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed is a method of preparing a thiohydrazide product compound from a hydrazide starting compound. The hydrazide starting compound is represented by Structural Formula (I): ##STR1##

The thiohydrazide product compound is represented by Structural Formula (II): ##STR2##

In Structural Formulas (I)-(II), R.sub.1 and R.sub.2 are independently an aliphatic group, a substituted aliphatic group, an aryl group or a substituted aryl group, or R.sub.1 and R.sub.2 taken together with the carbon and nitrogen atoms to which they are bonded, form a non-aromatic heterocyclic ring optionally fused to an aromatic ring. When R.sub.2 is an aryl group or a substituted aryl group, then R.sub.5 is a hydrazine protecting group; and when R.sub.2 is an aliphatic or substituted aliphatic group, then R.sub.5 is --H or a hydrazine protecting group. R.sub.10 is --H or a substituted or unsubstituted alkyl group. The method comprising the step of reacting the starting compound with a thionylating reagent.

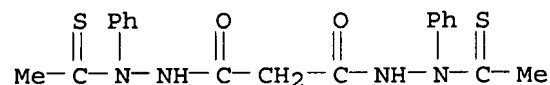
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 488831-49-8P 488831-53-4P 488831-54-5P
488831-55-6P 488831-56-7P 488831-57-8P
488831-58-9P

(process for preparation of bis(thiohydrazide) derivs. used as Taxol enhancers)

RN 488831-49-8 USPATFULL

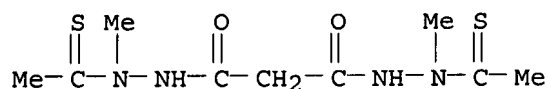
CN Propanedioic acid, 1,3-bis[2-phenyl-2-(1-thioxoethyl)hydrazide] (CA INDEX NAME)



RN 488831-53-4 USPATFULL

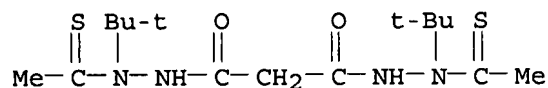
CN Propanedioic acid, 1,3-bis[2-methyl-2-(1-thioxoethyl)hydrazide] (CA INDEX NAME)

NAME)



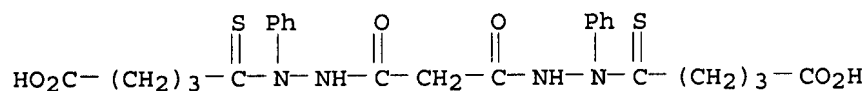
RN 488831-54-5 USPATFULL

CN Propanedioic acid, 1,3-bis[2-(1,1-dimethylethyl)-2-(1-thioxoethyl)hydrazide] (CA INDEX NAME)



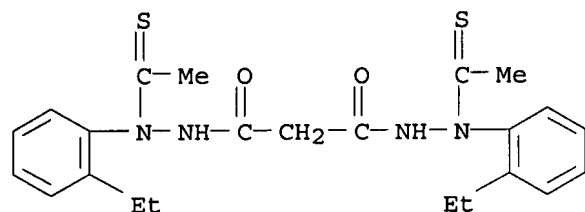
RN 488831-55-6 USPATFULL

CN Propanedioic acid, bis[2-(4-carboxy-1-thioxobutyl)-2-phenylhydrazide] (9CI) (CA INDEX NAME)



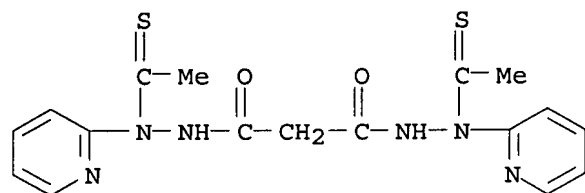
RN 488831-56-7 USPATFULL

CN Propanedioic acid, bis[2-(2-ethylphenyl)-2-(1-thioxoethyl)hydrazide] (9CI) (CA INDEX NAME)



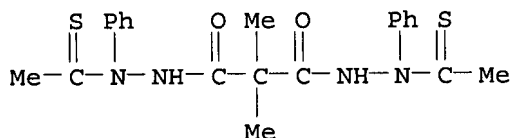
RN 488831-57-8 USPATFULL

CN Propanedioic acid, bis[2-(2-pyridinyl)-2-(1-thioxoethyl)hydrazide] (9CI) (CA INDEX NAME)



RN 488831-58-9 USPATFULL

CN Propanedioic acid, dimethyl-, bis[2-phenyl-2-(1-thioxoethyl)hydrazide] (9CI) (CA INDEX NAME)



L5 ANSWER 5 OF 5 USPATFULL on STN

ACCESSION NUMBER: 2003:65394 USPATFULL

TITLE: Taxol enhancer compounds

INVENTOR(S): Koya, Keizo, Brookline, MA, UNITED STATES
 Sun, Lijun, Harvard, MA, UNITED STATES
 Chen, Shoujun, Billerica, MA, UNITED STATES
 Tatsuta, Noriaki, Lexington, MA, UNITED STATES
 Wu, Yaming, Lexington, MA, UNITED STATES
 Ono, Mitsunori, Lexington, MA, UNITED STATES
 Xia, Zhi-Qiang, Dedham, MA, UNITED STATES

PATENT ASSIGNEE(S): Shionogi BioResearch Corp., Lexington, MA, UNITED STATES (U.S. corporation)

| | NUMBER | KIND | DATE | |
|---------------------|----------------|------|----------|------|
| PATENT INFORMATION: | US 2003045518 | A1 | 20030306 | <-- |
| | US 6762204 | B2 | 20040713 | |
| APPLICATION INFO.: | US 2002-193639 | A1 | 20020710 | (10) |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2001-304252P | 20010710 (60) |
| | US 2002-361936P | 20020306 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133 | |
| NUMBER OF CLAIMS: | 125 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 26 Drawing Page(s) | |
| LINE COUNT: | 2092 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB One embodiment of the present invention is a compound represented by the Structural Formula (I): ##STR1##

Y is a covalent bond of a substituted or unsubstituted straight chained hydrocarbaryl group. In addition, Y, taken together with both >C=Z groups to which it is bonded, is a substituted or unsubstituted aromatic group. Preferably, Y is a covalent bond or --C(R.sub.7R.sub.8)--.

R.sub.1 is an aliphatic group, a substituted aliphatic group, a non-aromatic heterocyclic group, or a substituted non-aromatic heterocyclic group, R.sub.2-R.sub.4 are independently --H, an aliphatic group, a substituted aliphatic group, a non-aromatic heterocyclic group, a substituted non-aromatic heterocyclic group, an aryl group or a substituted aryl group, or R.sub.1 and R.sub.3 taken together with the carbon and nitrogen atoms to which they are bonded, and/or R.sub.2 and R.sub.4 taken together with the carbon and nitrogen atoms to which they are bonded, form a non-aromatic heterocyclic ring optionally fused to an aromatic ring.

R.sub.5-R.sub.6 are independently --H, an aliphatic group, a substituted aliphatic group, an aryl group or a substituted aryl group.

R.sub.7 and R.sub.8 are each independently --H, an aliphatic or substituted aliphatic group, or R.sub.7 is --H and R.sub.8 is a

substituted or unsubstituted aryl group, or, R.sub.7 and R.sub.8, taken together, are a C2-C6 substituted or unsubstituted alkylene group.

Z is .dbd.O or .dbd.S.

Also disclosed are pharmaceutical compositions comprising the compound of the present invention and a pharmaceutically acceptable carrier or diluent.

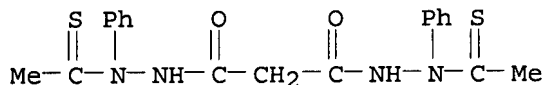
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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488831-55-6P 488831-56-7P 488831-57-8P
488831-58-9P 488831-60-3P 488831-61-4P
488831-65-8P

(preparation of bis(thiohydrazide) derivs. as Taxol enhancer compds. for the treatment of cancer)

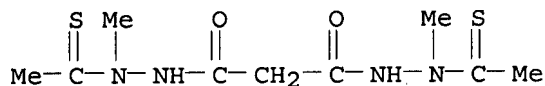
RN 488831-49-8 USPATFULL

CN Propanedioic acid, 1,3-bis[2-phenyl-2-(1-thioxoethyl)hydrazide] (CA INDEX NAME)



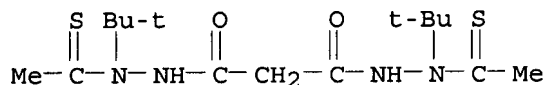
RN 488831-53-4 USPATFULL

CN Propanedioic acid, 1,3-bis[2-methyl-2-(1-thioxoethyl)hydrazide] (CA INDEX NAME)



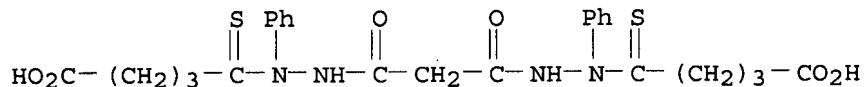
RN 488831-54-5 USPATFULL

CN Propanedioic acid, 1,3-bis[2-(1,1-dimethylethyl)-2-(1-thioxoethyl)hydrazide] (CA INDEX NAME)



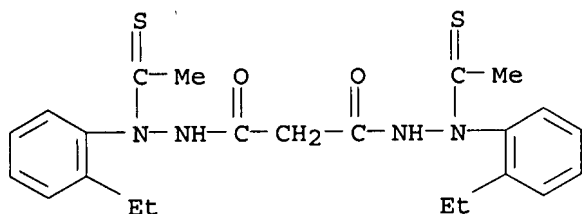
RN 488831-55-6 USPATFULL

CN Propanedioic acid, bis[2-(4-carboxy-1-thioxobutyl)-2-phenylhydrazide] (9CI) (CA INDEX NAME)



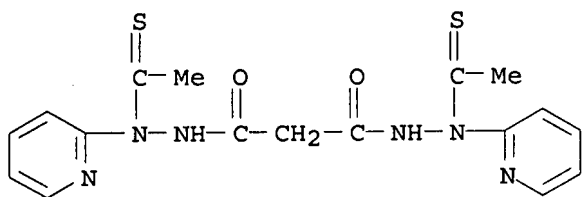
RN 488831-56-7 USPATFULL

CN Propanedioic acid, bis[2-(2-ethylphenyl)-2-(1-thioxoethyl)hydrazide] (9CI) (CA INDEX NAME)



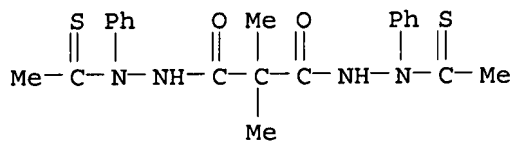
RN 488831-57-8 USPATFULL

CN Propanedioic acid, bis[2-(2-pyridinyl)-2-(1-thioxoethyl)hydrazide] (9CI)
(CA INDEX NAME)



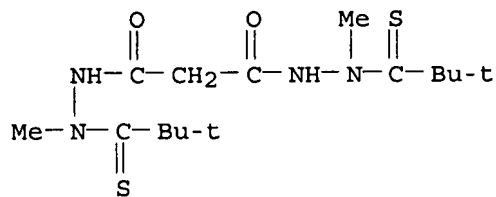
RN 488831-58-9 USPATFULL

CN Propanedioic acid, dimethyl-, bis[2-phenyl-2-(1-thioxoethyl)hydrazide]
(9CI) (CA INDEX NAME)



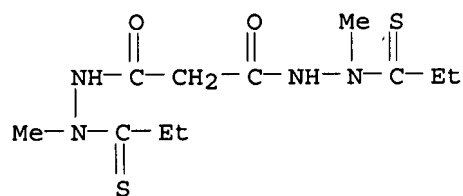
RN 488831-60-3 USPATFULL

CN Propanedioic acid, 1,3-bis[2-(2,2-dimethyl-1-thioxopropyl)-2-methylhydrazide] (CA INDEX NAME)

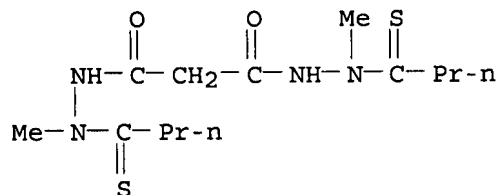


RN 488831-61-4 USPATFULL

CN Propanedioic acid, 1,3-bis[2-methyl-2-(1-thioxopropyl)hydrazide] (CA INDEX NAME)



RN 488831-65-8 USPATFULL
 CN Propanedioic acid, 1,3-bis[2-methyl-2-(1-thioxobutyl)hydrazide] (CA INDEX NAME)



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 FULL ESTIMATED COST

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
 CA SUBSCRIBER PRICE

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STRUCTURE FILE UPDATES: 11 SEP 2007 HIGHEST RN 946658-01-1
 DICTIONARY FILE UPDATES: 11 SEP 2007 HIGHEST RN 946658-01-1

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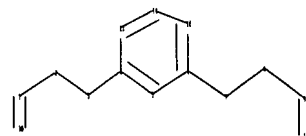
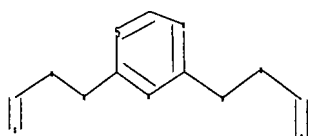
TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

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1  2  3  7  8  9 10 11
ring nodes :
4  5  6 13 14 16
chain bonds :
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ring bonds :
4-5  4-13 5-6  6-16 13-14 14-16
exact/norm bonds :
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G1:O,S

G2:CH,N

Match level :

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10:CLASS 11:CLASS 13:CLASS 14:CLASS 16:CLASS

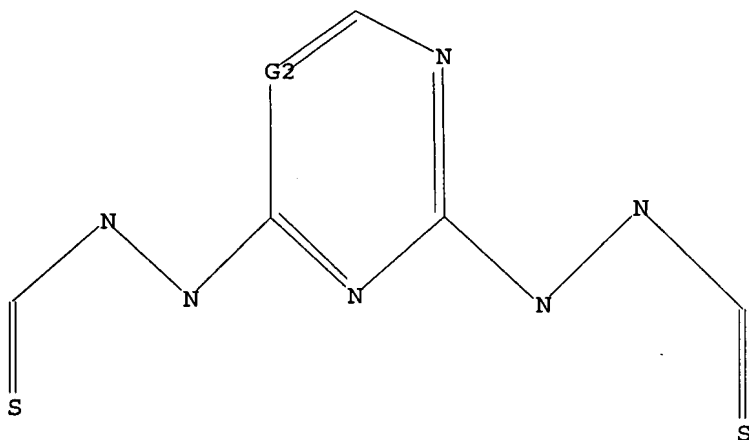
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L6 STRUCTURE UPLOADED

=> d 16

L6 HAS NO ANSWERS

L6 STR



G1 O,S
G2 CH,N

Structure attributes must be viewed using STN Express query preparation.

=> s 16 full
FULL SEARCH INITIATED 15:48:13 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 16 TO ITERATE

100.0% PROCESSED 16 ITERATIONS 7 ANSWERS
SEARCH TIME: 00.00.01

L7 7 SEA SSS FUL L6

=> file medline caplus wpids uspatfull
COST IN U.S. DOLLARS

FULL ESTIMATED COST

| SINCE FILE | TOTAL |
|------------|---------|
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

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| ENTRY | SESSION |
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FILE 'MEDLINE' ENTERED AT 15:48:24 ON 12 SEP 2007

FILE 'CAPLUS' ENTERED AT 15:48:24 ON 12 SEP 2007
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=> s 17
SAMPLE SEARCH INITIATED 15:48:29 FILE 'WPIDS'
SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**
PROJECTED ITERATIONS: 0 TO 0
PROJECTED ANSWERS: 0 TO 0

L8 2 L7

=> d l8 1-2 ibib, abs, hitstr

L8 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:94240 CAPLUS

DOCUMENT NUMBER: 140:248689

TITLE: Synthesis, chemical structure and photochemical and growth-regulating activity of some new 2,4-bis(alkyl/aryl-thiosemicarbazido)pyrimidines

AUTHOR(S): Vassilev, G. N.

CORPORATE SOURCE: Institute of Organic Chemistry, Bulgarian Academy of Sciences, Sofia, 1113, Bulg.

SOURCE: Oxidation Communications (2003), 26(4), 614-618

CODEN: OXCODW; ISSN: 0209-4541

PUBLISHER: SciBulCom Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:248689

AB Some new 2,4-bis(alkyl/aryl-thiosemicarbazido)pyrimidines were synthesized and the interrelation between the chemical structure, photochem. activity and plant-growth-regulating activity of the substances was investigated. For wheat root growth, all compds. showed inhibitory activity at 10⁻³ and 10⁻⁴ M and stimulating activity at 10⁻⁵ and 10⁻⁶ M. For cucumber, the compds., were stimulatory at all concns. The photochem. activity on pea chloroplast Hill reaction was in agreement with the data on wheat growth-regulating activity.

IT 77112-81-3P 77112-82-4P 77112-83-5P

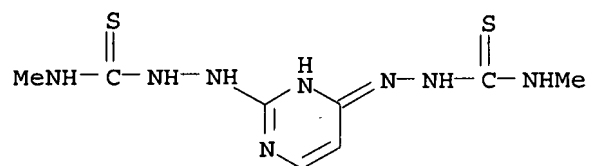
77112-84-6P 77112-85-7P 77112-86-8P

RL: AGR (Agricultural use); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation, plant-growth-regulating and Hill-reaction-inhibiting activity of)

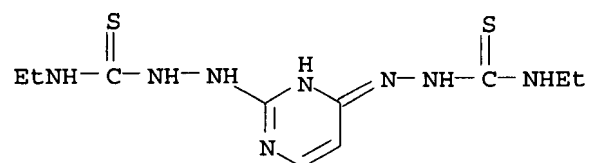
RN 77112-81-3 CAPLUS

CN Hydrazinecarbothioamide, 2,2'-(2,4-pyrimidinediyl)bis[N-methyl- (9CI) (CA INDEX NAME)



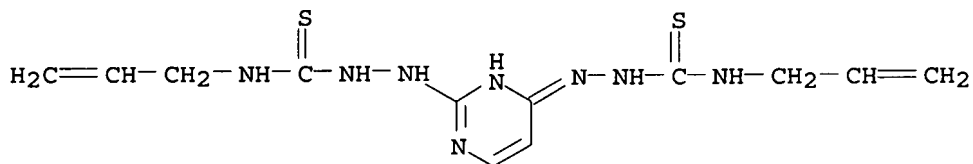
RN 77112-82-4 CAPLUS

CN Hydrazinecarbothioamide, 2,2'-(2,4-pyrimidinediyl)bis[N-ethyl- (9CI) (CA INDEX NAME)



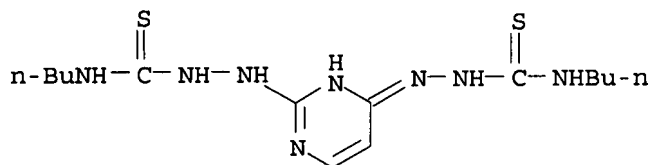
RN 77112-83-5 CAPLUS

CN Hydrazinecarbothioamide, 2,2'-(2,4-pyrimidinediyl)bis[N-2-propenyl- (9CI)
(CA INDEX NAME)



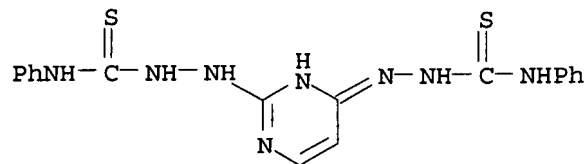
RN 77112-84-6 CAPLUS

CN Hydrazinecarbothioamide, 2,2'-(2,4-pyrimidinediyl)bis[N-butyl- (9CI) (CA
INDEX NAME)



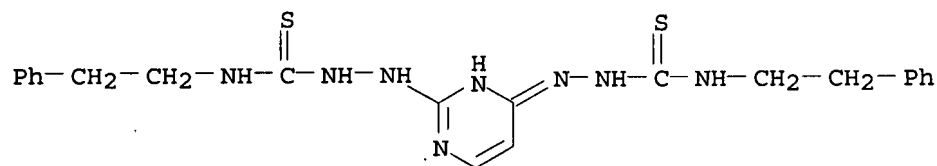
RN 77112-85-7 CAPLUS

CN Hydrazinecarbothioamide, 2,2'-(2,4-pyrimidinediyl)bis[N-phenyl- (9CI) (CA
INDEX NAME)



RN 77112-86-8 CAPLUS

CN Hydrazinecarbothioamide, 2,2'-(2,4-pyrimidinediyl)bis[N-(2-phenylethyl)-
(9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:139740 CAPLUS

DOCUMENT NUMBER: 94:139740

TITLE: Synthesis of 2-thiosemicarbazidopyrimidines and
2,4-uracil-bis(thiosemicarbazides)

AUTHOR(S): Vasilev, G.; Spasovska, N.; Spasov, A.

CORPORATE SOURCE: Inst. Plant Physiol., Sofia, 1113, Bulg.

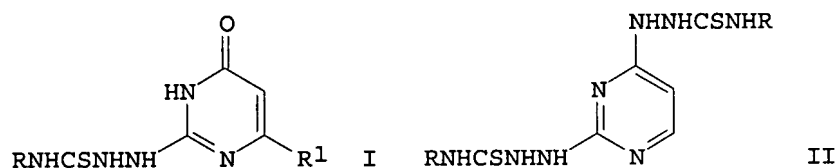
SOURCE: Doklady Bolgarskoi Akademii Nauk (1980), 33(6), 849-51
CODEN: DBANAD; ISSN: 0366-8681

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S):
GI

CASREACT 94:139740

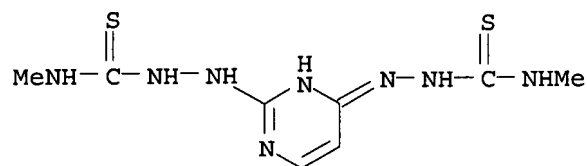


AB Thiosemicarbazides I and II (R = Me, Et, allyl, Bu, Ph, CH₂CH₂Ph; R₁ = H, Me) were obtained quant. by treating the hydrazines with RNCS. I and II stimulate or inhibit plant growth, depending on concentration. They also affect the Hill reaction (no data).

IT 77112-81-3P 77112-82-4P 77112-83-5P
77112-84-6P 77112-85-7P 77112-86-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

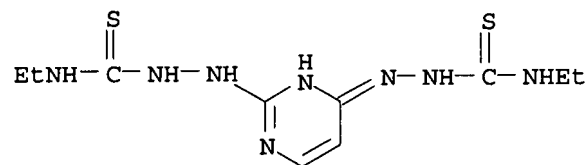
RN 77112-81-3 CAPLUS

CN Hydrazinecarbothioamide, 2,2'-(2,4-pyrimidinediyl)bis[N-methyl- (9CI) (CA INDEX NAME)



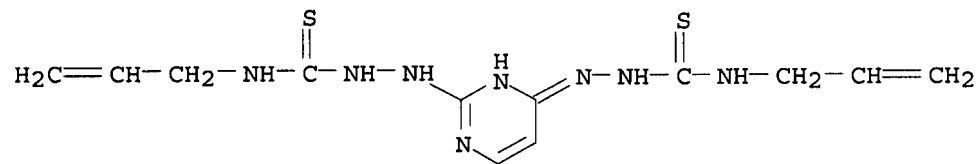
RN 77112-82-4 CAPLUS

CN Hydrazinecarbothioamide, 2,2'-(2,4-pyrimidinediyl)bis[N-ethyl- (9CI) (CA INDEX NAME)



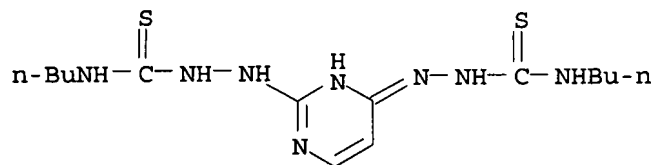
RN 77112-83-5 CAPLUS

CN Hydrazinecarbothioamide, 2,2'-(2,4-pyrimidinediyl)bis[N-2-propenyl- (9CI) (CA INDEX NAME)

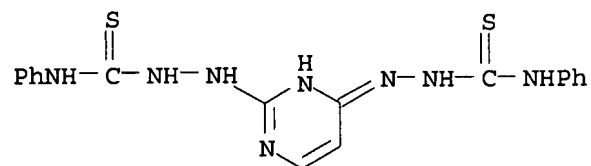


RN 77112-84-6 CAPLUS

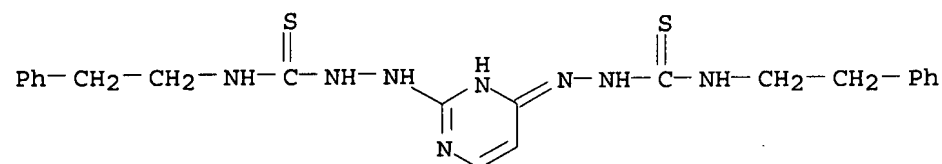
CN Hydrazinecarbothioamide, 2,2'-(2,4-pyrimidinediyl)bis[N-butyl- (9CI) (CA INDEX NAME)



RN 77112-85-7 CAPLUS
 CN Hydrazinecarbothioamide, 2,2'-(2,4-pyrimidinediyl)bis[N-phenyl- (9CI) (CA INDEX NAME)



RN 77112-86-8 CAPLUS
 CN Hydrazinecarbothioamide, 2,2'-(2,4-pyrimidinediyl)bis[N-(2-phenylethyl)- (9CI) (CA INDEX NAME)



=> d his

(FILE 'HOME' ENTERED AT 15:40:28 ON 12 SEP 2007)

FILE 'REGISTRY' ENTERED AT 15:40:40 ON 12 SEP 2007

L1 STRUCTURE UPLOADED

L2 17 S L1 FULL

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 15:41:45 ON 12 SEP 2007

L3 24 S L2

L4 21 S L3 AND (?CANCER? OR ?TUMOR?)

L5 5 S L4 AND PY<2004

FILE 'REGISTRY' ENTERED AT 15:47:57 ON 12 SEP 2007

L6 STRUCTURE UPLOADED

L7 7 S L6 FULL

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 15:48:24 ON 12 SEP 2007

L8 2 S L7

=>

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=> LOG Y

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